

Illum is relied upon as describing "polystyrene microspheres having a diameter of 5.25 micrometers coated with poloxamer." As described in column 2 of the patent, the particle is coated wherein the coating has a thickness of about 100 Angstrom or larger. At column 3, the patent describes measuring the thickness of the coating layers. The fact that the microspheres are coated is critical to the objective of the invention, which is designed to minimize liver up-take. The particles described in the patent are not embraced within the claims.

The claimed invention relates to particles which have a low density, such as a tap density less than 0.4 g/cm³, a mean diameter between approximately 5 and 30 microns, and an aerodynamic diameter between approximately one and five microns. Dense, non-porous microparticles are not embraced by the claims.

Illum describes 5.25 micron particles which carry an additional coating. According to the Illum invention, an absorbed layer thickness of about 230 Angstroms is necessary. Column 4, lines 59-63. The polystyrene microspheres (typically obtained as beads, versus a light powder) were coated by incubating them in a 2% w/v solution of POLOXAMINE 908. More typically, the polystyrene microspheres are in the size range of 50-60 nm with a coating of about 134 Angstrom (Example 1). There is nothing in the reference which teaches or suggests that the particles described therein possess the density or aerodynamic diameter of the claimed particles.

A generic or non-specific disclosure of a product or products cannot generally support a rejection under anticipation. See, for example, *Ex parte A*, 17 USPQ2d 1716 (BPAI 1990), *In re Petering*, 133 USPQ 275 (CCPA 1962), *In re Meyer*, 202 USPQ 175 (CCPA 1979). The reference described herein does not describe particles having the specified mass mean diameter, density and aerodynamic diameter with the particularity required to "at once envisage" the claims. *In re Petering, supra*.

Furthermore, the claims, as amended, do not embrace polymeric microspheres. Withdrawal of the rejection is requested.

Rejection under 35 U.S.C. 102(b) over Yen, U.S. Patent No. 5,069,936

Claims 1, 4, 6, and 9-14 are rejected under 35 U.S.C. 102(b) over Yen, U.S. Patent No. 5,069,936. Applicants respectfully disagree.

Yen is relied upon as describing protein microspheres containing protein, drug and a surfactant. The particles described in the patent are not embraced within the claims.

The claimed invention relates to particles which have a low density, such as a tap density less than 0.4 g/cm³, a mean diameter between approximately 5 and 30 microns, and an aerodynamic diameter between approximately one and five microns. Particles characterized by a sub-micron mean diameter are not embraced within the claims. The claims, as amended, claim particles consisting of therapeutic agent and a surfactant or complexing agent. The claims do not embrace crosslinked proteinaceous microspheres.

Rejection under 35 U.S.C. 102(e) and 35 U.S.C. 103 over Baichwal, U.S. Patent No. 5,612,053

Claims 1-5, 9-15, 17-20, 24-30 and 32-33 are rejected under 35 U.S.C. 102(e) and Claims 1-33 are rejected under 35 U.S.C. 103 over Baichwal, U.S. Patent No. 5,612,052 and prior art cited in the specification. Applicants respectfully disagree.

Baichwal teach drug compositions for inhalation therapy. While the reference does appear to teach the selection of particles possessing a mass mean diameter below 10 diameters, , the reference does not teach that delivery can be improved by optimizing the density of the particle and, thereby, the aerodynamic diameter. Furthermore, Baichwal teaches compositions characterized by a polysaccharide gum carrier, not embraced within the claims.

Rejection under 35 U.S.C. 103 over Masinde (Intl. J. Pharm.)in view of Illum

Claims 1-33 are rejected under 35 U.S.C. 103 over Masinde in view of Illum. Applicants respectfully disagree.

Masinde is relied upon to teach PLGA microspheres. Illum is cited to teach the addition of a surfactant. As discussed above, the claimed invention does not embrace polymeric microspheres, The references do not teach or describe particles having a density or aerodynamic diameter within the range described in the claims. Furthermore, the reference does not teach that pulmonary delivery can be improved by optimizing the density of the particle and, thereby, the aerodynamic diameter. Thus, the references, which provide no more than a generic or non-specific disclosure of various drug compositions cannot support a rejection under anticipation. In re Petering, *supra* The references described herein do not describe particles having the specified mass mean diameter, density and aerodynamic diameter with the particularity required to "at once envisage" the claims. In re Petering, *supra*. Furthermore, Masinde and Illum teach compositions characterized by a polymer carrier, not embraced within the claims.

Withdrawal of the rejections is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

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